CASE REPORT

Pulmonary sarcoidosis shortly after spinal tuberculosis infection: a diagnostic challenge

Julian A Luetkens,¹ Shahram Zoghi,² Jürgen K Rockstroh,² Claas P Naehle¹

¹Department of Radiology, University of Bonn, Bonn, Germany

²Department of Internal Medicine I, University of Bonn, Bonn, Germany

Correspondence to
Dr Claas P Naehle,
cp@naehle.net

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SUMMARY

Tuberculosis and sarcoidosis share similar histopathological findings. An aetiological connection between these diseases has been discussed. We report a case of pulmonary sarcoidosis, which occurred shortly after an isoniazid (INH)-resistant spinal tuberculosis was diagnosed which was suspected to be a miliary tuberculosis. This report illustrates the need to sensitise clinicians to two possible important causes of lung parenchyma alterations under tuberculostatic therapy.

BACKGROUND

Sarcoidosis is a multisystem disease of unknown aetiology characterised by non-caseating granulomas, which can involve any organ. The most common manifestation is pulmonary sarcoidosis with enlargement of intrathoracic lymph nodes in approximately 90% of the cases.¹ Different microorganisms, including *Mycobacterium tuberculosis*, have been described as possible aetiological agents of sarcoidosis.² Because tuberculosis and sarcoidosis are similar in their histopathological findings, sarcoidosis is an important differential diagnosis to tuberculosis. In this article, we report—to our

knowledge—the first case of a miliary pulmonary sarcoidosis occurring shortly after isoniazid (INH)-resistant spinal tuberculosis infection.

CASE PRESENTATION

A 37-year-old male paramedic presented at our clinic with weight loss, night sweats, fever and severe back pain. There was no medical history. An MRI of the spine showed a left-sided psoas abscess as well as inflammatory destruction of TH 6/7 and L 1/2 consistent with tuberculous spondylodisitis (figure 1). CT-guided abscess drainage and an antimicrobial susceptibility test were performed. Acid-fast stain of the abscess material was negative for mycobacteria. Microbiological tests detected *Streptococcus acidominimus*, and antibiotic therapy was initiated. Interferon- γ release assays were positive. Three weeks later the mycobacterial culture of the abscess material was positive for *M tuberculosis*. A multi-drug therapy consisting of INH, pyrazinamide, rifampicin and ethambutol was started. As clinical improvement did not ensue, a second CT-guided drain was placed to improve drainage. In the meantime, susceptibility testing revealed INH-resistance and INH was replaced by

Figure 1 MRI showing spondylodisitis at TH 6/7 and L 1/2 with pronounced thoracic deformation (spliced sequences from left to right: fat suppressed T2-weighted, contrast-enhanced T1-weighted, T1 subtraction imaging).

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streptomycin leading to an improvement of the patient's general condition. However, because lower back pain still persisted, a follow-up MRI of the lower spine was performed, which revealed an aggravation of the inflammatory destruction of the spine. Vertebrectomy and internal fixation were performed, and with supportive physiotherapy the patient recovered well from this operation. After 2 months of tuberculostatic therapy streptomycin was discontinued. Eight weeks after this adjustment follow-up imaging studies discovered new multiple fine nodular densities distributed throughout both lungs (figure 2). Because of suspected miliary tuberculosis moxifloxacin was added to the pharmacological regime; however, the radiological pulmonary manifestations became worse on follow-up chest X-rays. Remarkably, the patient had no constitutional symptoms, was feeling well, and anaemia and C reactive protein-elevations had resolved under tuberculostatic therapy, beyond that repetitive interferon- γ release assays were negative—contrary to expectations. Further diagnostic workup including bronchoscopy was performed. The CD4/CD8 ratio in the bronchoalveolar lavage was 7 (normal range: 1.1–3.5) and bronchial biopsy showed non-caseating granulomas with no tubercle bacilli (figure 3), leading to the diagnosis of new-onset sarcoidosis. ACE testing revealed elevated enzyme levels and biopsy tissue culture showed no growth of *M tuberculosis*. Pulmonary function tests showed a restrictive ventilatory dysfunction consistent with incipient lung fibrosis. Systemic corticosteroid therapy was initiated, which led to the improvement of lung function and observed radiological findings.

Figure 2 Chest CT scan upon admission (A), and during follow-up (B). After surgical treatment and initiation of tuberculostatic therapy, multiple fine nodular densities occurred throughout both lungs.

Figure 3 Bronchial biopsy specimen showing non-caseating epithelioid granuloma with peripheral cicatrization consistent with sarcoidosis (H&E).

OUTCOME AND FOLLOW-UP

The patient has remained on a combination of antituberculous and corticosteroid therapy. Physical therapy was also initiated. The patient reported no problems during the last follow-ups, and lung parenchyma alterations dissolved on follow-up chest X-rays after 4 months.

DISCUSSION

Infectious agents have long been suspected as possible causes of sarcoidosis. In our case, the sequential occurrence of tuberculosis and miliary sarcoidosis points to a similar immunological mechanism. Because of their histopathological resemblance, a possible aetiological link between tuberculosis and sarcoidosis has often been discussed, and there is an increasing evidence that *M tuberculosis* might account for at least some cases of sarcoidosis.³ In addition, molecular studies using liquid-phase hybridisation and PCR provided evidence of mycobacterial genes in sarcoid tissue^{4 5}; and remnant *M tuberculosis* catalase-peroxidase (mKatG) has been identified as a possible target of the adaptive immune response in sarcoidosis.⁶ Interestingly, a sequential occurrence of sarcoidosis as presented in our case remains rare given the overall frequency of tuberculosis. In fact, a PubMed-based literature research revealed only seven clinical reports of sarcoidosis following an active tuberculosis infection since 2000.⁷

The occurrence of new fine nodular opacifications on our patient's chest X-ray films were initially interpreted as miliary tuberculosis. Miliary tuberculosis results from haematogenous dissemination of tubercle bacilli, and is a disease with a high mortality.⁸ Clinically, patients are severely ill with pronounced constitutional symptoms. When severe symptoms are absent and tuberculosis seems to progress in spite of an efficient treatment as in our patient, alternative causes of micronodular lung parenchyma alterations (ie, sarcoidosis, metastatic disease, lymphoma or septic emboli) should be considered.⁹ Especially, new onset of sarcoidosis should be considered if pathological findings in imaging studies persist in spite of anti-tubercular therapy. Though systemic corticosteroid therapy is the medication of choice in symptomatic sarcoidosis,¹ it may turn out to be a disadvantage in patients with miliary tuberculosis.

In our patient, the diagnosis of sarcoidosis was established because bronchial biopsy showed non-caseating granulomas, CD4/CD8 ratio in the bronchoalveolar lavage was elevated, ACE levels were elevated and culture on the biopsy tissue did

not reveal any evidence of *M tuberculosis*. Because sarcoidosis is often a diagnosis of exclusion it is mandatory to exclude alternative diagnoses.³

Although a strong molecular and clinical evidence for an association between sarcoidosis and tuberculosis is still lacking, our report is intended to increase awareness of the possible temporal coexistence of these two diseases.

Learning points

- ▶ Sarcoidosis and miliary tuberculosis can present with the same radiological pattern on chest X-ray and chest CT.
- ▶ If a tuberculosis infection seems to progress in spite of an efficient treatment, it is important to consider alternative causes of similar lung parenchyma alterations, for example, the occurrence of sarcoidosis.
- ▶ Although there is some evidence for an aetiological connection between tuberculosis and sarcoidosis, a sequential occurrence remains rare.

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critically for important intellectual content, made a final approval of the version to be published and made an agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. JAL and SZ made substantial contributions to the acquisition, analysis, or interpretation of data for the work and drafted the work.

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